The association between gestational diabetes mellitus and postpartum depressive symptomatology : A prospective cohort study

Ruohomäki, Aleksi

2018-12-01

Ruohomäki , A , Toffol , E , Upadhyaya , S , Keski-Nisula , L , Pekkanen , J , Lampi , J , Voutilainen , S , Tuomainen , T-P , Heinonen , S , Kumpulainen , K , Pasanen , M & Lehto , S M 2018 , ' The association between gestational diabetes mellitus and postpartum depressive symptomatology : A prospective cohort study ' , Journal of Affective Disorders , vol. 241 , pp. 263-268 . https://doi.org/10.1016/j.jad.2018.08.070

http://hdl.handle.net/10138/305683
https://doi.org/10.1016/j.jad.2018.08.070

publishedVersion

Journal of Affective Disorders 241 (2018) 263–268

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

The association between gestational diabetes mellitus and postpartum depressive symptomatology: A prospective cohort study

Aleksi Ruohomäki[a,*], Elena Toffol[b,c], Subina Upadhyaya[d], Leea Keski-Nisula[e,f], Juha Pekkanen[g,h], Jussi Lampi[g,i], Sari Voutilainen[j], Tomi-Pekka Tuomainen[j], Seppo Heinonen[k,l], Kirsti Kumpulainen[m], Markku Pasanen[n], Soili M. Lehto[a,b,o,p]

[a] Institute of Clinical Medicine / Psychiatry, University of Eastern Finland, Kuopio, Finland
[b] Department of Psychology and Logopedics, Faculty of Medicine, University of Helsinki, Helsinki, Finland
[c] Department of Public Health Solutions, National Institute for Health and Welfare, Helsinki, Finland
[d] Research Centre for Child Psychiatry, University of Turku, Turku, Finland
[e] Department of Obstetrics and Gynaecology, Kuopio University Hospital, Kuopio, Finland
[f] Department of Health Sciences, Clinical Medicine, University of Eastern Finland, Kuopio, Finland
[g] Department of Health Protection, National Institute for Health and Welfare, Kuopio, Finland
[h] Department of Public Health, University of Helsinki, Helsinki, Finland
[i] Social and Health, City of Kuopio, Kuopio, Finland
[j] Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland
[k] Department of Obstetrics and Gynaecology, University of Helsinki, Helsinki, Finland
[l] Department of Obstetrics and Gynaecology, Helsinki University Hospital, Helsinki, Finland
[m] Institute of Clinical Medicine / Child Psychiatry, University of Eastern Finland, Kuopio, Finland
[n] Faculty of Health Sciences, School of Pharmacy, University of Eastern Finland, Kuopio, Finland
[o] Department of Psychiatry, Faculty of Medicine, University of Helsinki, Helsinki, Finland
[p] Department of Psychiatry, Kuopio University Hospital, Kuopio, Finland

ARTICLE INFO

Keywords:
Gestational diabetes mellitus
Peripartum depressive symptomatology
Postpartum depressive symptomatology

ABSTRACT

Background: The literature suggests an association between type 2 diabetes mellitus and depression, but data on the association between gestational diabetes mellitus (GDM) and postpartum depressive symptomatology (PPDS) are scarce.

Methods: Altogether, 1066 women with no previous mental health issues enrolled in the Kuopio Birth Cohort (KuBiCo, www.kubico.fi) were selected for this study. GDM was diagnosed according to the Finnish Current Care Guidelines. Depressive symptomatology was assessed with the Edinburgh Postnatal Depression Scale (EPDS) during the third trimester of pregnancy and eight weeks after delivery. Additionally, a subgroup of women (n = 505) also completed the EPDS during the first trimester of pregnancy.

Results: The prevalence rates of GDM and PPDS in the whole study population were 14.1% and 10.3%, respectively. GDM was associated with an increased likelihood of belonging to the PPDS group (OR 2.23, 95% CI 1.23–4.05; adjusted for maternal age at delivery, BMI in the first trimester, smoking before pregnancy, relationship status, nulliparity, delivery by caesarean section, gestational age at delivery, neonatal intensive care unit admission and third-trimester EPDS scores). A significant association between GDM and PPDS was found in the subgroup of women with available data on first-trimester depression (n = 505).

Limitations: The participation rate of the KuBiCo study was relatively low (37%).

Conclusions: Women with GDM may be at increased risk of PPDS. Future studies should investigate whether these women would benefit from a closer follow-up and possible supportive interventions during pregnancy and the postpartum period to avoid PPDS.

Abbreviations: GDM, gestational diabetes mellitus; EPDS, Edinburgh Postnatal Depression Scale; NICU, neonatal intensive care unit; PPD, postpartum depression; PPDS, postpartum depressive symptomatology

* Corresponding author at: Institute of Clinical Medicine / Psychiatry, University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland.
E-mail address: aleksiru@student.uef.fi (A. Ruohomäki).

https://doi.org/10.1016/j.jad.2018.08.070
Received 26 March 2018; Received in revised form 25 June 2018; Accepted 12 August 2018
Available online 15 August 2018
0165-0327/

1. Introduction

Gestational diabetes mellitus (GDM) and postpartum depression (PPD) are both highly prevalent in perinatal conditions. In Finland, during the last five years, the 12-month prevalence of GDM has been reported to be approximately 9–13% (National Institute of Health and Welfare, 2016), and worldwide, the respective figures have been as high as 17.8% (Coustan et al., 2010). Nevertheless, the prevalence of GDM has varied in the literature due to inconsistent diagnostic criteria and study populations (Mcintyre et al., 2015). GDM usually develops before the third trimester of pregnancy, and is caused by insufficient secretion of insulin with respect to overt gestational insulin resistance, a physiological condition that all pregnant women develop to some degree (Buchanan and Xiang, 2005). Furthermore, approximately 10–15% of all mothers are affected by PPD (Patel et al., 2012). PPD represents a possible risk to a healthy mother–baby relationship, and may thus have a significant impact on infant development (Tronick and Reck, 2009).

Several potential risk factors for PPD have been identified, such as a history of depression before pregnancy, depression or anxiety during pregnancy and poor social support (O'Hara and McCabe, 2013). Furthermore, obesity at the beginning of pregnancy has been suggested to increase the likelihood of PPD (Molyneaux et al., 2014), and PPD has been suggested to be a preface to a chronic depressive disorder (Vliegen et al., 2014). In turn, high pre-pregnancy BMI and excessive weight gain during early pregnancy are associated with a significantly increased risk of GDM (Morisset et al., 2010; Robitaille, 2015). Women with GDM are also at greater risk of developing type 2 diabetes mellitus later in life (Bellamy et al., 2009).

In the general population, people with type 2 diabetes mellitus have a 21% greater risk of experiencing depressive symptoms than those without type 2 diabetes (Nouwen et al., 2010). Conversely, people with a diagnosis of depression or with depressive symptoms have a 1.4-fold greater risk of developing type 2 diabetes mellitus than non-diagnosed or asymptomatic individuals (Knol et al., 2006). Furthermore, an association between a medical history of depression and an increased likelihood of developing GDM has been suggested based on a large multi-ethnic retrospective cohort study in the US (Bowers et al., 2013). Nevertheless, data on the relationship between GDM and PPD remain scarce.

A recent population-based study has suggested an association between GDM and a subsequent diagnosis of depression within the first year after delivery (Silverman et al., 2017). The diagnostic criteria for GDM were not reported as part of this study (Silverman et al., 2017). Furthermore, a prospective cohort study suggested an association between GDM and postpartum depressive symptomatology (PPDS) at six weeks after delivery (Hinkle et al., 2016). However, no significant association between GDM and PPDS at six months after delivery was detected in another recent study (Huang et al., 2015). Nevertheless, this study used different diagnostic criteria for GDM compared to our study (Huang et al., 2015).

Thus, we sought to clarify the association between GDM and PPDS in a prospective setting, using GDM diagnostic criteria closely resembling the established International Association of Diabetes and Pregnancy Study Groups criteria for GDM. Based on the few previous epidemiological observations and the similar adverse immunological changes in both GDM and PPDS (Osborne and Monk, 2013), we hypothesized that GDM would be associated with an increased likelihood of belonging to the group with PPDS compared to the group with no PPDS.

2. Methods

2.1. Study sample

This study was conducted as a part of the ongoing Kuopio Birth Cohort (KuBiCo; www.kubico.fi) Study. The KuBiCo Study was initiated in 2012, with a target of collecting data from a total of 10,000 mother–child pairs until the child reaches the age of 18 years. All women who are expected to give birth at Kuopio University Hospital based on their place of residence are invited to participate in the study. To date, the participation rate has been approximately 37%. The research ethics committee of the Central Finland Health Care District has approved the KuBiCo study (8.12.2011, K-S SHP Dnro 18U/2011).

The sample used in this study was extracted from the KuBiCo database in January 2017 (n = 4145) and included all pregnancies that had complete Edinburgh Postnatal Depression Scale (EPDS) data in the postpartum phase (n = 1917). Of these pregnancies, the final sample consisted of a total of 1066 women after the exclusion of later pregnancies of women who provided more than one case (n = 50) and those women with previous mental health issues (n = 174), a previous diagnosis of diabetes mellitus (n = 38), multiple pregnancy (n = 19), missing information on EPDS in the third trimester of pregnancy (n = 652), missing information on age (n = 4) or missing information on BMI in the first trimester (n = 9). Data on previous diagnoses of diabetes mellitus were based on self-reports in cases of type I diabetes (n = 19), type II diabetes (n = 7) and GDM in previous pregnancies (n = 5). In the case of self-reports of undefined types of diabetes (n = 7), the diagnoses were checked from hospital records to distinguish between previously diagnosed diabetes and current GDM. Data on multiple pregnancies were retrieved from hospital records, and the previous mental health issues were either self-reported as a part of routine Finnish prenatal care as “previous mental health issues / psychiatric disorder” (n = 156) or based on the self-reported earlier use of psychotropic medication (n = 66). In attrition analysis, no differences were detected between the group excluded from the original sample and the group with full available data either in the mean ranks of BMI in the first trimester (means: final sample 24.8 kg/m^2 vs. excluded 24.9 kg/m^2; Z = –0.4, p = 0.674) or in the mean ranks of maternal age at delivery (means: final sample 30.1 years vs. excluded 29.9 years; Z = –0.7, p = 0.481). Of the final sample, a sub-group of 505 women had also completed the EPDS during the first trimester of pregnancy, and they were included in the secondary analyses.

2.2. Gestational diabetes mellitus

GDM was diagnosed according to Finnish clinical guidelines as a routine procedure, on average during pregnancy weeks 24–28 (Finnish Current Care Guidelines, www.kaypahoito.fi). All participants underwent an oral glucose tolerance test (OGTT), with the following two exceptions defined by the clinical guidelines: 1) young (< 25 years) nulliparous women with BMI < 25 kg/m^2 whose close relatives (siblings, parents or grandparents) had not had type 2 diabetes mellitus (American Diabetes Association, 2007) and 2) multiparous women under 40 years of age and with BMI < 25 kg/m^2 whose earlier pregnancies had been free from GDM and foetal macrosomia (Lu et al., 2002). For the above exceptions, as well as for individuals with normal earlier OGTT values, an OGTT was in some cases performed or repeated later during pregnancy due to some other clinical GDM risk indicators, such as excessive maternal weight gain or foetal growth, or an increased amount of amniotic fluid. In our study population, 79% of the women underwent an OGTT during some stage of their pregnancy, and 20% of the women underwent the test twice. The OGTT was administered in the morning after a 12-hour fast. In the OGTT, a venous blood sample is taken before drinking 300 ml of water containing 75 g of glucose within five minutes. Second and third venous blood samples are taken one and two hours after ingesting the test liquid. Diagnostic thresholds for elevated plasma glucose concentrations are as follows: 5.3 mmol/l for the fasting stage, 10.0 mmol/l for 1 h after ingesting the test liquid and 8.6 mmol/l for 2 hours after ingesting the test liquid. Meeting or exceeding at least one of the above set values is considered diagnostic for GDM. The diagnoses of GDM were retrieved from hospital diagnosis records.

Table 1
Characteristics of the study population in relation to gestational diabetes mellitus.

	GDM = no (n = 916, 85.9%)	GDM = yes (n = 150, 14.1%)	Test value	p-value
		n (%)		
Postpartum depressive symptomatology	86 (9.4)	24 (16.0)	$\chi^2 = 6.1$	0.014[a]
Caesarean section	86 (9.4)	23 (15.3)	$\chi^2 = 5.0$	0.026[a]
Neonatal intensive care unit admission	86 (9.4)	19 (12.7)	$\chi^2 = 1.6$	0.212[a]
Nulliparous	512 (55.9)	71 (47.3)	$\chi^2 = 3.8$	0.051[a]
Smoking before pregnancy	121 (13.2)	16 (10.7)	$\chi^2 = 0.7$	0.388[a]
Living with a partner	335 (36.6)	54 (36.0)	$\chi^2 = 0.02$	0.893[a]
Third-trimester depressive symptomatology	88 (9.6)	13 (8.7)	$\chi^2 = 0.1$	0.715[a]
		Mean (SD)		
BMI in the first trimester (kg/m^2)	24.1 (4.3)	28.7 (6.5)	$Z = -8.8$	<0.001[b]
Maternal age at delivery (years)	29.9 (4.9)	31.4 (5.4)	$Z = -3.3$	0.001[b]
Gestational age at delivery (weeks)	39.6 (1.5)	39.3 (1.4)	$Z = -2.5$	0.011[b]

[a] Chi-squared test.
[b] Mann–Whitney U-test.

2.3. Depression

Third-trimester depressive symptomatology and postpartum depressive symptomatology (PPDS) were assessed with the EPDS, which is completed online between weeks 28 and 44 of pregnancy and eight weeks after delivery. Additionally, a total of 505 women also completed the EPDS during the first trimester between pregnancy weeks 6 and 13. The EPDS is a 10-item questionnaire with four response options for each question. Each answer is scored on a scale of 0–3 points, and the final scale score ranges between 0 and 30. A cut-off of 10 points or more was used to identify women with depressive symptomatology (Cox et al., 1987). In this article, we use the depressive symptomatology cut-off to define first-trimester depressive symptomatology, third-trimester depressive symptomatology and PPDS.

2.4. Covariates

Based on previous literature on the risk factors for both GDM and PPD, covariates for our models included: maternal age at delivery (continuous) (Reid and Meadows-Oliver, 2007), BMI (kg/m^2) in the first trimester (continuous) (Molyneaux et al., 2014), the relationship status (living with a partner vs. not living with a partner) (Dørheim et al., 2009), nulliparity (yes/no) (Räisänen et al., 2013) and smoking before pregnancy (smoked one or more cigarettes per day vs. zero cigarettes per day) (Lasser et al., 2000), collected with a background questionnaire completed online by the mothers in the first trimester of their pregnancy. Additional covariates consisted of gestational age at delivery (weeks) (Räisänen et al., 2013), mode of delivery (vaginal or caesarean delivery) (Räisänen et al., 2013) and the need for neonatal intensive care unit (NICU) admission (Blom et al., 2010), as entered by a nurse into an electronic database on the delivery ward at Kuopio University Hospital.

2.5. Statistical methods

Univariate differences between women with and without GDM were evaluated using the chi-squared test for dichotomous variables and Mann–Whitney U-test for continuous variables due to their non-normal distribution. Normality was assessed with a normal Q–Q plot and histogram visualisation. In order to examine the possible mediator role of the covariates, we also determined univariate differences between the PPDS group and the non-PPDS group using the chi-squared test for dichotomous variables and Mann–Whitney U-test for continuous variables.

2.5.1. Multivariable analyses for the whole study population

To investigate the effect of potential confounders on the observed associations between GDM and PPDS, we utilised logistic regression analysis (method: enter). After determining the crude OR, three different models were constructed. Model 1 included maternal age at delivery and BMI in the first trimester. Model 2 included all the variables in the study except for third-trimester EPDS scores (i.e., maternal age at delivery, BMI in the first trimester, smoking before pregnancy, relationship status, nulliparity, delivery by caesarean section, gestational age at delivery and NICU admission). Model 3 was Model 2 further adjusted for third-trimester EPDS scores.

2.5.2. Multivariable analyses for the subgroup of women with complete first-trimester EPDS data

Separate logistic regression analyses were performed in the subgroup of women who also completed the EPDS during the first trimester of pregnancy. In order to avoid overfitting, among this subgroup, the maximum number of covariates was limited to 5, i.e. to 10% or less of the number of subjects in the smallest group under observation (PPDS group, n = 50) (Babyak, 2004). Thus, for these analyses, Model 4 was Model 1 (maternal age at delivery and first trimester BMI) further adjusted for first-trimester EPDS scores, and Model 5 was Model 4 further adjusted for third-trimester EPDS scores.

All the statistical tests were two-tailed, with the alpha level set to 0.05. IBM SPSS Statistics Version 24 was used to analyse the data.

3. Results

3.1. All participants

In the whole study population (n = 1066), the prevalence rates of GDM and PPDS were 14.1% (n = 150) and 10.3% (n = 110), respectively. Women with GDM had a higher prevalence of PPDS and the mode of delivery was more often caesarean section compared to women with no GDM (Table 1). Women in the GDM group were also older and their BMI in the first trimester was higher than among women in the non-GDM group. Among women with GDM, the gestational age at delivery was lower than among those with no GDM.

Furthermore, of the women with PPDS, 40.9% (n = 45) had third-trimester depressive symptomatology. In the whole sample, the prevalence of third-trimester depressive symptomatology was 9.5% (n = 101) (of these women, 44.6% (n = 45) subsequently developed PPDS). GDM was not associated with an increased likelihood of third-trimester depressive symptomatology (OR 0.89, 95% CI 0.49–1.64).

Of the covariates included in the analyses, four lay chronologically between the GDM diagnosis and the PPDS measurement (i.e., third-trimester depressive symptomatology, gestational age, caesarean section and NICU admission). However, only caesarean section and gestational age were in fact associated with GDM (Table 1), thus implying their possible role as mediators. However, this possibility was ruled out, as these variables were not associated with PPDS (prevalence of PPDS

Table 2
Likelihood of women with a diagnosis of gestational diabetes mellitus belonging to the group with postpartum depressive symptomatology in logistic regression models performed in the whole study population (n = 1066).

	Odds ratio	95% Confidence interval	p-value
Unadjusted	1.84	1.13–3.00	0.015
Model 1	1.70	1.00–2.89	0.048
Model 2	1.83	1.08–3.11	0.026
Model 3	2.23	1.23–4.05	0.008

Model 1 is adjusted for maternal age at delivery and BMI in the first trimester.
Model 2 is Model 1 further adjusted for smoking before pregnancy, living with a partner, nulliparity, gestational age at delivery, caesarean section and neonatal intensive care unit admission.
Model 3 is Model 2 further adjusted for third-trimester EPDS scores.

in caesarean section group vs. vaginal delivery group: 10.1% vs. 10.3%, $\chi^2 = 0.01$; $p = 0.934$; mean gestational age in non-PPDS vs. PPDS group: 39.5 weeks vs. 39.7 weeks, $Z = -0.8$, $p = 0.420$). In the multivariable analysis, GDM was associated with a 1.7-fold higher likelihood of belonging to the group with PPDS (adjusted for maternal age at delivery and BMI in the first trimester: OR 1.70, 95% CI 1.00–2.89) (Table 2). This association remained significant in all further adjustment models and was most robust in Model 3, which included all the available covariates (OR 2.23, 95% CI 1.23–4.05).

3.2. Women with complete first-trimester EPDS data

In the subgroup of women who completed the EPDS during the first trimester (n = 505), the prevalence rates of GDM and depressive symptomatology were as follows: GDM 14.7% (n = 74), first-trimester depressive symptomatology 7.5% (n = 38), third-trimester depressive symptomatology 8.1% (n = 41) and PPDS 9.9% (n = 50). In this subgroup, of the women with PPDS, 26.0% (n = 13) had first-trimester depressive symptomatology, 36.0% (n = 18) had third-trimester depressive symptomatology, 48.0% (n = 24) had either first-trimester or third-trimester depressive symptomatology, or both, and 14.0% (n = 7) had both first-trimester and third-trimester depressive symptomatology. Neither first-trimester depressive symptomatology (OR 0.48, 95% CI 0.14–1.60) nor third-trimester depressive symptomatology (OR 1.00, 95% CI 0.40–2.46) was associated with an increased likelihood of belonging to the GDM group. The crude association between GDM and PPDS was significant in the chi-squared test (prevalence of PPDS in non-GDM group vs. GDM group: 8.8% vs. 16.2%, $\chi^2 = 3.9$, $p = 0.049$) and nearly significant in unadjusted logistic regression analysis (OR: 2.00, 95% CI 0.99–4.04) (Table 3). However, the association was no longer significant after adjusting for maternal age at delivery and BMI in the first trimester alone (Model 1): OR 1.82, 95% CI 0.86–3.87. Nevertheless, the association between GDM and an increased likelihood of belonging to the PPDS group remained significant in all further adjustment models and was most robust in Model 5, which included maternal age at delivery, BMI in the first trimester, first-trimester EPDS scores and third-trimester EPDS scores as covariates (OR 2.43, 95% CI 1.05–5.62).

Table 3
Likelihood of women with a diagnosis of gestational diabetes mellitus belonging to the group with postpartum depressive symptomatology in logistic regression models performed in the subgroup of women with complete first-trimester EPDS data (n = 505).

	Odds ratio	95% Confidence interval	p-value
Unadjusted	2.00	0.99–4.04	0.053
Model 1	1.82	0.86–3.87	0.117
Model 4	2.34	1.06–5.17	0.036
Model 5	2.43	1.05–5.62	0.039

Model 1 is adjusted for maternal age at delivery and BMI in the first trimester.
Model 4 is Model 1 further adjusted for first-trimester EPDS scores.
Model 5 is Model 4 further adjusted for third-trimester EPDS scores.

4. Discussion

4.1. Main findings

We observed an association between GDM and a higher risk of PPDS, irrespective of third-trimester depressive symptomatology. Furthermore, among the subgroup of women with complete EPDS data for both first and third trimesters, first-trimester depressive symptomatology was not associated with an elevated risk of subsequent GDM, and the observation of an association between GDM and a higher risk of PPDS was significant when controlling for first-trimester depressive symptomatology.

4.2. Comparison with previous literature

Our finding of an association between a diagnosis of GDM and a higher risk of PPDS is consistent with the results of a prospective cohort study in the US (Hinkle et al., 2016), a population-based prospective cohort study in Sweden (Silverman et al., 2017) and a longitudinal cohort study in an Iranian population (Abdollahi et al., 2014). The US study used different diagnostic criteria (i.e., the Carpenter and Coustan criteria (Mcintyre et al., 2015)) compared with the present study. This resulted in a noticeable difference in the prevalence of GDM between the US study group and the present study group (4.3% vs. 14.1%, respectively). Furthermore, the US study found an association between depressive symptomatology in early pregnancy and an increased risk of GDM, whereas in our study, first-trimester depressive symptomatology was not associated with an increased likelihood of subsequent GDM. Nevertheless, the GDM criteria were not specified in either the Swedish study or the Iranian study, and the observations derived from these studies were not controlled for maternal BMI at the beginning of pregnancy, a crucial potential confounding factor.

Despite the above findings being in line with our observations, five other studies have found no associations between GDM and PPD/PPDS (Huang et al., 2015; Kim et al., 2005; Liu and Tronick, 2013; Meltzer-Brody et al., 2017; Miller et al., 2016). However, it is notable that the only one of these five studies to specify the diagnostic criteria for GDM used the two-step method recommended by the American Diabetes Association (Huang et al., 2015). The difference in GDM prevalence between the study groups in this US longitudinal study (Huang et al., 2015) and in the current study (5.2% vs. 14.1%, respectively) is in line with that reported in a study comparing the two-step approach criteria with the IADPSG criteria (6% with the two-step approach vs. 14.5% with the IADPSG criteria) (Sevket et al., 2014). Thus, it remains uncertain whether it is possible to compare the longitudinal US study (Huang et al., 2015) with our study, considering the noticeable difference in the criteria used to diagnose GDM. However, one of the five studies with no observed association between GDM and PPD/PPDS found an association between GDM and the postpartum acute stress reaction (Meltzer-Brody et al., 2017). Moreover, one cross-sectional study examined the relationship between GDM and PPDS in two ethnically different populations: an association was observed among Qatari women, while no such association was observable among other Arab women (Burgut et al., 2013). Unfortunately, no information on the maternal BMI or the diagnostic criteria of GDM was available for this study (Burgut et al., 2013).

4.3. Possible mechanisms

Psychological factors may at least partly explain the observed association between GDM and PPDS. The diagnosis of GDM may be considered as a stressful life event, which itself is an established risk

factor for PPD (O'Hara and McCabe, 2013). From the point of view of physiological mechanisms, abnormal glucose metabolism might partially induce dysregulation of the hypothalamic–pituitary–adrenal axis and increase cytokine-mediated inflammatory responses, which are considered to be associated with depression (Moulton et al., 2015). Such changes might lead, for example, to decreased serotonin production in the central nervous system (Moulton et al., 2015). This hypothesis is partly supported by previous evidence of a link between insulin resistance and depression (Kan et al., 2013): this finding suggests at least a partial contribution of direct physiological mechanisms, considering that insulin resistance is not associated with a relevant psychological burden, as is the case in overt diabetes. In addition, chronic insulin resistance at some level has been suggested to contribute to the development of GDM (Buchanan and Xiang, 2005), which in turn was associated with PPDS in our study.

4.4. Strengths and limitations

In the attrition analyses, we detected no differences in BMI in the first trimester or maternal age at delivery between women excluded from the analyses and our final sample. Thus, the final sample can be considered to be representative of the whole extracted sample. Furthermore, the availability of additional measures of depressive symptomatology during pregnancy (in the third trimester for the whole sample, and in both the first and third trimesters for the sub-sample) allowed us to control for the possible role of earlier-onset depressive symptomatology, which is a strength of this study. An additional strength is the explicitly defined OGTT to identify GDM; this approach is comparable with the testing recommended by the IADPSG panel, and uses similar thresholds and analogous procedures (Coustan et al., 2010).

Some limitations need to be taken into consideration while interpreting the findings of this study.

The participation rate in the KuBiCo study is relatively low (37%), possibly due to the long duration of the whole study (approximately 19 years). Thus, even though all the women who were expected to give birth at Kuopio University Hospital, with no exclusions, were invited to participate in the study, the presence of a selection bias cannot be ruled out. Furthermore, having access to measurements of glycated haemoglobin would have allowed undiagnosed cases of pre-pregnancy diabetes to be detected, and would thus have improved the precision of this study. However, adjusting multivariable models for BMI in the first trimester, a variable very likely to correlate strongly with pre-pregnancy diabetes, did not alter our final observations. Thus, it is unlikely that undiagnosed pre-pregnancy diabetes biased our findings. Additionally, information on the clinical diagnoses of PPD would have further supplemented information derived from the EPDS questionnaire to identify PPDS. Nevertheless, the utilized EPDS questionnaire is a well-established measure for investigating PPDS (Cox et al., 1987).

5. Conclusions

This study suggests that GDM is associated with a higher likelihood of PPDS, irrespective of depressive symptomatology during pregnancy. Future studies should investigate whether these women would benefit from a closer follow-up and possible supportive interventions during pregnancy and the postpartum period to prevent PPDS. Furthermore, the underlying mechanism of this association remains to be explored. It would be beneficial to resolve whether the psychological burden related to the GDM diagnosis is a significant part of these mechanisms. If this is the case, adopting new diagnostic criteria for GDM, which would potentially increase the prevalence of GDM, would simultaneously increase the prevalence of PPDS.

Contributors

All the authors participated substantially in the design of the study. Data analyses were carried out by A.R. and interpretations of the analyses were conducted by A.R. and S.M.L. A.R. wrote the first draft of the manuscript and all the authors critically revised it for important intellectual content. All the authors have approved the final version to be published.

Role of the funding source

The KuBiCo study received funding from the Research Committee of the Kuopio University Hospital Catchment Area for State Research Funding (project 5302475, Kuopio, Finland), and from the Ministry of Social Affairs and Health, Finland. ET was supported by funding from the Finnish Medical Foundation and the Jalmari and Rauha Ahokas Foundation. SML was supported by funding from the Paulo Foundation and the Finnish Medical Foundation. The funding sources had no involvement in the following: the study design; the collection, analysis and interpretation of the data; the writing of the report; or the decision to submit the article for publication.

Institutional review board approval

The research ethics committee of Central Finland Health Care District has approved the KuBiCo study (8.12.2011, K-S SHP Dnro 18U/2011).

Conflict of interest

None.

Acknowledgement

The authors wish to thank all the KuBiCo mothers for participating in this study.

References

Abdollahi, F., Zarghami, M., Azhar, M.Z., Sazlina, S.-G., Lye, M.-S., 2014. Predictors and incidence of post-partum depression: a longitudinal cohort study. J. Obstet. Gynaecol. Res. 40, 2191–2200. https://doi.org/10.1111/jog.12471.

American Diabetes Association, 2007. Diagnosis and classification of diabetes mellitus. Diab. Care 30, S42–S47. https://doi.org/10.2337/dc07-S042.

Babyak, M.A., 2004. What you see may not be what you get: A brief, nontechnical introduction to overfitting in regression-yype models. Psychosom. Med. 66, 411–421.

Bellamy, L., Casas, J., Hingorani, A.D., Williams, D., 2009. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 373, 1773–1779. https://doi.org/10.1016/S0140-6736(09)60731-5.

Blom, E.A., Jansen, P.W., Verhulst, F.C., Hofman, A., Raat, H., Jaddoe, V.W.V, Coolman, M., Steegers, E.A.P., Tiemeier, H., 2010. Perinatal complications increase the risk of postpartum depression. The generation R study. BJOG 117, 1390–1398. https://doi.org/10.1111/j.1471-0528.2010.02660.x.

Bowers, K., Laughon, S.K., Kim, S., Mumford, S.L., Brite, J., Kiely, M., Zhang, C., 2013. The association between a medical history of depression and gestational diabetes in a large multi-ethnic cohort in the United States. Paediatr. Perinat. Epidemiol. 27, 323–328. https://doi.org/10.1111/ppe.12057.

Buchanan, T.A., Xiang, A.H., 2005. Gestational diabetes mellitus. J. Clin. Invest. 115, 485–491.

Burgut, F.T., Bener, A., Ghuloum, S., Sheikh, J., 2013. A study of postpartum depression and maternal risk factors in Qatar. J. Psychosom. Obstet. Gynaecol. 34, 90–97. https://doi.org/10.3109/0167482X.2013.786036.

Coustan, D.R., Lowe, L.P., Metzger, B.E., Dyer, A.R., 2010. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study: paving the way for new diagnostic criteria for gestational diabetes mellitus. Am. J. Obstet. Gynecol. 202 (654), e1–e6. https://doi.org/10.1016/j.ajog.2010.04.006.

Cox, J.L., Holden, J.M., Sagovsky, R., 1987. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J. Psychiatry 150, 782–786.

Dørheim, S.K., Bondevik, G.T., Eberhard-Gran, M., Bjorvatn, B., 2009. Sleep and depression in postpartum women: a population-based study. Sleep 32, 847–855.

Hinkle, S.N., Louis Buck, G.M., Rawal, S., Zhu, Y., Albert, P.S., Zhang, C., 2016. A longitudinal study of depression and gestational diabetes in pregnancy and the postpartum period. Diabetologia 59, 2594–2602. https://doi.org/10.1007/s00125-

016-4086-1.
Huang, T., Rifas-Shiman, S.L., Ertel, K.A., Rich-Edwards, J., Kleinman, K., Gillman, M.W., Oken, E., James-Todd, T., 2015. Pregnancy hyperglycaemia and risk of prenatal and postpartum depressive symptoms. Paediatr. Perinat. Epidemiol. 29, 281–289. https://doi.org/10.1111/ppe.12199.
Kan, C., Silva, N., Golden, S.H., Rajala, U., Timonen, M., Stahl, D., Ismail, K., 2013. A systematic review and meta-analysis of the association between depression and insulin resistance. Diabetes Care. 36, 480–489. https://doi.org/10.2337/dc12-1442.
Kim, C., Brawarsky, P., Jackson, R.A., Fuentes-Afflick, E., Haas, J.S., 2005. Changes in health status experienced by women with gestational diabetes and pregnancy-induced hypertensive disorders. J. Womens Health (Larchmt) 14, 729–736.
Knol, M.J., Twisk, J.W.R., Beekman, A.T.F., Heine, R.J., Snoek, F.J., Pouwer, F., 2006. Depression as a risk factor for the onset of type 2 diabetes. A meta-analysis. Diabetologia 49, 837–845. https://doi.org/10.1007/s00125-006-0159-x.
Lasser, K., Boyd, J.W., Woolhandler, S., Himmelstein, D.U., Mccormick, D., Bor, D.H., 2000. Smoking and mental illness: a population-based prevalence study. JAMA 284, 2606–2610.
Liu, C.H., Tronick, E., 2013. Rates and predictors of postpartum depression by race and ethnicity: results from the 2004 to 2007 New York City PRAMS survey (Pregnancy Risk Assessment Monitoring System). Matern Child Health J. 17, 1599–1610. https://doi.org/10.1007/s10995-012-1171-z.
Lu, G.C., Luchesse, A., Chapman, V., Cliver, S., Rouse, D.J., 2002. Screening for gestational diabetes mellitus in the subsequent pregnancy: is it worthwhile? Am. J. Obstet. Gynecol. 187, 918–921. https://doi.org/10.1067/mob.2002.126979.
Mcintyre, H.D., Colagiuri, S., Roglic, G., Hod, M., 2015. Diagnosis of GDM: a suggested consensus. Best Pract. Res. Clin. Obstet. Gynaecol. 29, 194–205. https://doi.org/10.1016/j.bpobgyn.2014.04.022.
Meltzer-Brody, S., Maegbaek, M.L., Medland, S.E., Miller, W.C., Sullivan, P., Munk-Olsen, T., 2017. Obstetrical, pregnancy and socio-economic predictors for new-onset severe postpartum psychiatric disorders in primiparous women. Psychol. Med. 47, 1427–1441. https://doi.org/10.1017/S0033291716003020.
Miller, E.S., Peri, M.R., Gossett, D.R., 2016. The association between diabetes and postpartum depression. Arch. Womens. Ment. Health 19, 183–186. https://doi.org/10.1007/s00737-015-0544-x.
Molyneaux, E., Poston, L., Ashurst-Williams, S., Howard, L.M., 2014. Obesity and mental disorders during pregnancy and postpartum: a systematic review and meta-analysis. Obstet. Gynecol. 123, 857–867. https://doi.org/10.1097/AOG.0000000000000170.
Morisset, A.-S., St-yves, A., Veillette, J., Weisnagel, J.S., Tchernof, A., Robitaille, J., 2010. Prevention of gestational diabetes mellitus: a review of studies on weight management. Diabetes Metab. Res. Rev. 26, 17–25. https://doi.org/10.1002/dmrr.
Moulton, C.D., Pickup, J.C., Ismail, K., 2015. The link between depression and diabetes: the search for shared mechanisms. Lancet. Diabetes Endocrinol. 3, 461–471. https://doi.org/10.1016/S2213-8587(15)00134-5.
Nouwen, A., Winkley, K., Twisk, J., Lloyd, C.E., Peyrot, M., Ismail, K., Pouwer, F., 2010. Type 2 diabetes mellitus as a risk factor for the onset of depression: a systematic review and meta-analysis. Diabetologia 53, 2480–2486. https://doi.org/10.1007/s00125-010-1874-x.
O'Hara, M.W., McCabe, J.E., 2013. Postpartum depression: current status and future directions. Annu. Rev. Clin. Psychol. 9, 379–407. https://doi.org/10.1146/annurev-clinpsy-050212-185612.
Osborne, L.M., Monk, C., 2013. Perinatal depression - The fourth inflammatory morbidity of pregnancy? Theory and literature review. Psychoneuroendocrinology 38, 1929–1952. https://doi.org/10.1016/j.psyneuen.2013.03.019.
Patel, M., Bailey, R.K., Jabeen, S., Ali, S., Barker, N.C., Osiezagha, K., 2012. Postpartum depression: a review. J. Health Care Poor Underserved 23, 534–542. https://doi.org/10.1353/hpu.2012.0037.
Räisänen, S., Lehto, S.M., Nielsen, H.S., Gissler, M., Kramer, M.R., Heinonen, S., 2013. Fear of childbirth predicts postpartum depression: a population-based analysis of 511 422 singleton births in Finland. BMJ Open 3, e004047. https://doi.org/10.1136/bmjopen-2013-004047.
Reid, V., Meadows-Oliver, M., 2007. Postpartum depression in adolescent mothers: an integrative review of the literature. J. Pediatr. Health Care 21, 289–298. https://doi.org/10.1016/j.pedhc.2006.05.010.
Robitaille, J., 2015. Excessive gestational weight gain and gestational diabetes: importance of the first weeks of pregnancy. Diabetologia 58, 2203–2205. https://doi.org/10.1007/s00125-015-3725-2.
Sevket, O., Ates, S., Uysal, O., Molla, T., Dansuk, R., Kelekci, S., 2014. To evaluate the prevalence and clinical outcomes using a one-step method versus a two-step method to screen gestational diabetes mellitus. J. Matern. Fetal Neonatal Med. 27, 36–41. https://doi.org/10.3109/14767058.2013.799656.
Silverman, M.E., Reichenberg, A., Savitz, D.A., Cnattingius, S., Lichtenstein, P., Hultman, C.M., Larsson, H., Sandin, S., 2017. The risk factors for postpartum depression: a population-based study. Depress. Anxiety 34, 178–187. https://doi.org/10.1002/da.22597.
Tronick, E., Reck, C., 2009. Infants of depressed mothers. Harv. Rev. Psychiatry 17, 147–156. https://doi.org/10.1080/10673220902899714.
Vliegen, N., Casalin, S., Luyten, P., 2014. The course of postpartum depression: a review of longitudinal studies. Harv. Rev. Psychiatry 22, 1–22. https://doi.org/10.1097/HRP.0000000000000013.